

or impart to the binding polymers, distinctive electrophoretic mobilities for separation and detection; thus, Grossman discloses the elements of Applicants' electrophoretic probes, except for capture ligands. Kline discloses an assay system employing a capture reagent comprising analyte-specific binding compounds attached to an anionic polymer. After analyte binds to the binding compounds (either displacing labeled analyte in the competitive format or further binding with a labeled antibody in the sandwich format), the entire complex is captured by an oppositely charged (cationic) solid phase. One of ordinary skill in the art would be motivated to add a biotin (or like capture ligand) to Applicants' electrophoretic probes in order to use an ion-capture reagent of Kline employing avidin (or like binding compound) to impart a charge to the probes opposite to that of the released eTag reporters of Applicants' invention.

Applicants respectfully disagree. Kline at most discloses an immunoassay employing a soluble capture reagent comprising multiple binding compounds, such as analyte-specific antibodies, bound to an anionic polymer. After incubation with a sample that contains analyte (and perhaps, in addition, labeled antibody when used in the sandwich format), the resulting negatively charged complex is captured with a positively charged solid phase (col. 6, lines 60-65) and removed from the reaction mixture (col. 18, line 64, to col. 19, line 4), where it is then detected (col. 19, lines 8-12). The thrust of Kline's invention is to provide a solution-phase analog to an enzyme-linked immunosorbent assay (ELISA) in order to avoid the difficulties of carrying out protein binding reactions near surfaces (col. 7, lines 4-11; also note that all detection in the examples is carried out enzymatically (alkaline phosphatase operating on a fluorogenic substrate)). In Kline, a charged capture reagent is combined with an oppositely charged solid phase to remove binding compound-analyte complexes from a reaction mixture for detection, whereas in Applicants' invention, charged capture agents are combined with unreacted electrophoretic probes and cleavage products thereof to give them a charge opposite of that of released eTag reporters so that they are not electrophoretically separated together. *That is, in Kline, a moiety is captured so that it can be detected, whereas, in Applicants' invention, a moiety is captured to prevent it from being detected.* Applicants' use of such charged capture agents results in a dramatic increase in resolution of electrophoretically separated eTag reporters, as illustrated in Figs. 26 and 27 of the application. Applicants submit that neither Kline nor Grossman, either alone or together, disclose or suggest, or provide motivation of, the concept of using charged capture agents to bind to *undesired* components of a reaction mixture to exclude them from being separated and detected with oppositely charged reporter molecules, thereby increasing the sensitivity of assay measurements.

In view of the above, Applicants submit that the cited references have been inappropriately combined and do not render Applicants' invention obvious to one of ordinary skill in the art. Accordingly, Applicants respectfully request that the rejection be withdrawn.

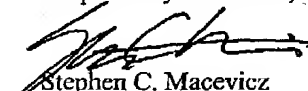
In paragraph 4 of the Office Action, the Examiner rejected claim 24 under 35 U.S.C. 103(a) as being unpatentable over Grossman (cited above) in view of Kline (cited above) and further in view of Ullman (U.S. patent 6,251,581). The Examiner applied Grossman and Kline as above and further argued that the specific structures recited in claim 29 are disclosed by the chemiluminescent compounds of Ullman.

Applicants respectfully disagree. First, as stated above, Applicants submit that Grossman and Kline have been inappropriately combined. Second, although Ullman discloses compounds similar to those recited in claim 24, the *compositions of Applicants' invention comprise pluralities of such compounds that form distinct peaks in an electropherogram upon electrophoretic separation*. Such compositions are neither disclosed nor suggested by Ullman. In fact, Ullman teaches away from such compositions because his objective is to provide a homogeneous assay based solely on optical (chemiluminescent) detection without any separation of the optically detected molecules; consequently, one of ordinary skill in the art would not be motivated to combine the teaching of Ullman with that of Grossman and Kline. Accordingly, Applicants respectfully request that the rejection be withdrawn.

In view of the above, Applicants submit that the claims as written fully satisfy the requirements of Title 35 of the U.S. Code, and respectfully request that the rejections thereunder be withdrawn and that the claims be allowed and the application quickly passed to issue.

If any additional time extensions are required, such time extensions are hereby requested. If any additional fees not submitted with this response are required, please take such fees from deposit account 50-2266.

Respectfully submitted,



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